REMARKS

This paper is responsive to the Final Office Action mailed October 9, 2003, setting an initial due date of January 9, 2004. This Response is accompanied by a Petition for Two-Month Extension of Time and requisite fee, extending the period for response to March 9, 2004, and accompanies the filing of a Request for Continued Examination.

Status of the Claims

In the Final Action, the Office indicated claims 1-10, 12-15, 38-47, and 50-57, were pending, of which claims 15 and 38-40 were withdrawn from consideration. With this amendment, claims 1-40 and 42-50 are canceled without prejudice or disclaimer, leaving claim 41 pending.

Rejections - 35 U.S.C. § 102(b)

The Office rejects claims 1, 2, 6-10, 12-14, 42-47, 52, and 56-57 under 35 U.S.C. § 102(b) as allegedly being anticipated by Schultz (U.S. Patent No. 5,162,218).[1]

Without acquiescing to the procedural propriety or substantive correctness of this final rejection, Applicants have canceled claims 1, 2, 6-10, 12-14, 42-47, 52, and 56-57, without prejudice or disclaimer. Thus, the rejection is moot.

Rejections - 35 U.S.C. § 103(a)

The Office rejects claims 41, 51, and 53-55 under 35 U.S.C. § 103(a) as being "unpatentable over Schultz (U.S. Patent No. 5,162,218) and in view of Nowinski et al. (U.S. Patent No. 4,711,840)." (Office Action, page 5, lines 1-2.)

In response, and without acquiescing to the procedural propriety or substantive correctness of this final rejection, Applicants note that claims 51 and 53-55 have been canceled

[1] Applicants respectfully note that the Office refers to 35 U.S.C. § 102(b) in the sentence summarizing the rejection on page 3 of the Action (lines 4-5). However, the section of the statute quoted immediately above in the Action is from 35 U.S.C. § 102(a). Because Schultz issued in 1992, the reference to 102(a) must have been in error.

without prejudice or disclaimer. Thus, the rejection is moot as it applies to those claims and Applicants will address the rejection as it relates to the sole remaining pending claim, claim 41.

Initially, Applicants note that the Office indicates claim 41 is "unpatentable over Schultz (U.S. Patent No. 5,162,218) *and* in view of Nowinski et al. (U.S. Patent No. 4,711,840)." (Office Action, page 5, lines 1-2; emphasis added.) However, the Office admits that Schultz "did not teach greater change in conformation as a result of an analyte binding to the biopolymer than that occurs in an individual monomeric unit as a result of binding to an analyte." (Office Action, sentence spanning pages 5-6.) Yet the Office fails to state why that missing element would have been obvious in view of Schultz alone. Beyond mentioning that Schultz fails to disclose that claimed element, the Action completely ignores it as it relates to Schultz.

As stated in the Manual of Patent Examining Procedure (M.P.E.P. § 2142), to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

In response to the rejection over Schultz alone, Applicants respectfully submit that Schultz does not teach or suggest the admittedly missing element. As admitted by the Office, Schultz does not teach a greater change from binding a biopolymer than by binding individual monomeric units, i.e., it does not teach all the claim limitations. Applicants submit that there is nothing in Schultz, or in the art generally, that would have led to this modification in Schultz's teaching. As Applicants' claim 41 includes elements that are not taught or suggested by Schultz, Applicants respectfully submit that Schultz does not render the claim obvious.

For the admittedly missing teaching, the Office relies on Nowinski. "Nowinski et al. teach analyte-specific incorporation of fluorescence into a polymer, wherein Nowinski et al.

teach a greater change in conformation, that is, a 20-fold increase in flurorescence *[sic]* as [a] result of analyte binding to the biopolymer as compared to a control (see [column] 15, lines 5-22). Nowinski et al. also teach reactant functional groups that bind to a biopolymer, which includes hydroxyl, amine, carboxy groups (see column 7, lines 17-67)."

The Office states that it would have been prima facie obvious to a person of ordinary skill in the art to combine the multimeric polypeptides as taught by Schultz with the teachings of Nowinski et al. to achieve the expected advantage of developing a multimeric biopolymer having a greater efficiency in binding. (Office Action, page 6, lines 8-11.) The Office concludes by stating that an ordinary practitioner would have been motivated to combine the multimeric biopolymer of Schultz with the limitations as taught by Nowinski et al. to improve the configuration of the synthetic multimeric biopolymer structure by including the greater change in conformation as taught by Nowinski et al. (Office Action, page 6, lines 15-18.)

Applicants respectfully submit that the Office appears to have misread the disclosure of Nowinski et al., and at least because of this misreading, the Office's reliance on Nowinski et al. for the missing teaching is misplaced.

Nowinski et al. teaches an immunoassay involving several components (see column 10, lines 32-59). First, a mouse monoclonal antibody, which binds to human IgM, is coupled to a monomer (2-hydroxyethyl methacrylate). A second mouse monoclonal antibody, which binds to a separate portion of human IgM than the first mouse monoclonal, is fluorescently labeled. In the presence of human IgM (the analyte), a ternary complex is formed between the first mouse monoclonal -- human IgM -- and the second mouse monoclonal. The sample fluoresces in an amount directly proportional to the amount of analyte in the sample. Because of the direct proportionality, the binding is quantitative for the amount of analyte in the sample.

The presence of reactive monomer on the first mouse monoclonal allows for an additional reaction. Upon the addition of additional free monomer, along with a polymerization catalyst, homopolymerization between monoclonal/monomer conjugates, or heteropolymerization between monoclonal/monomer conjugates and free monomers in solution, occurs, producing an insoluble polymer particle. Thus, when analyte (IgM) is also present, the

insoluble polymer particle fluoresces in an amount proportional to the amount of analyte present in the sample. If analyte is not present, the polymerized particles do not fluoresce. The particles can then be separated using known means or can be counted and their fluorescence quantified on a fluorescence-activated cell sorter ("FACS," a flow cytometer).

The second mouse monoclonal antibody, which is fluorescently labeled, is responsible for the increase in the fluorescent signal. Binding of this antibody to a single molecule of analyte, i.e., formation of a two-molecule complex, produces the fluorescent output. Binding of the first mouse monoclonal antibody, which is conjugated to the reactive monomer, should not impact fluorescence. Nor should the homo- or heteropolymerization between the conjugated reactive monomer and free monomer in solution to produce polymeric particles. Indeed, for the assay quantitatively to measure analyte concentration, neither binding of the antibody-monomer to the complex nor the subsequent polymerization should affected fluorescence output.

Polymerization in Nowinski et al. does not result in a conformational change that is measured. Rather, it produces an insoluble particle that can be separated. Therein lies Nowinski et al.'s purported advantage over existing methods that require a solid phase support: Nowinski et al.'s solid phase is formed in solution. Thus, when Nowinski et al. states that "polymers are of limited value in that the spacing and steric accessibility, and number of polypeptides bound per unit length of polymer cannot be precisely or reproducibly controlled," he is discussing the drawbacks of pre-formed solid phase supports. Nowinski et al.'s teaching has nothing whatsoever to do with increasing "efficiency in binding" or in producing a "greater change in conformation."

The Offices asserts that Nowinski et al.'s reference to a "20-fold increase in fluorescence intensity" as compared to control is reflective of a "greater change in conformation." (Office Action, page 6, lines 3-5.) With respect, Applicants submit that Nowinski et al. was comparing two samples: one with analyte, and one without, i.e., the "control." In both instances, polymerization occurred, producing insoluble particles. The presence of analyte simply produced fluorescent particles. As compared to the control sample, in which no analyte was present, the test sample exhibited a 20-fold increase in intensity. The increase in fluorescence intensity resulted from the interaction of analyte and its corresponding binding site on the mouse

monoclonal antibody. In the presence of excess monoclonal antibody, fluorescence intensity was directly proportional to the concentration of analyte. There is nothing in this example of Nowinski et al., or in any other part of Nowinski et al., that suggests that polymerization or a conformational change resulting therefrom, has any effect on signal intensity.

The pending claims require that the signal generated by the covalently linked monomeric units that comprise a binding region for an analyte, when the analyte is bound thereto, be greater than the signal generated by the monomeric units that comprise a binding region for an analyte not covalently linked to each other, when the analyte is bound thereto. In other words, a dimer binding analyte would exhibit greater signal than a monomer. (See, for example, Examples 1 and 2 on pages 17-18.) This concept is not taught or suggested by Nowinski et al.

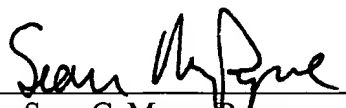
Applicants respectfully submit that there is no suggestion or motivation, either in Schultz, Nowinski et al., alone or combined, or in the knowledge generally available to one of ordinary skill in the art, to modify Schultz or to combine Schultz with Nowinski et al. The Office has attempted to explain why Nowinski et al. should be combined with Schultz, but it appears to have misread Nowinski et al.'s disclosure. Nowinski et al. simply does not stand for the teachings the Office attributes to it. It is respectfully submitted that claim 41 is not rendered obvious by the combination of Schultz with Nowinski et al.

In view of the foregoing remarks and amendments, Applicants respectfully submit that the claim under consideration is in condition for allowance. Applicants respectfully request the consideration and examination of this application, and prompt issuance of a Notice of Allowance.

The Examiner is invited to contact the undersigned attorney to discuss actions that may be taken to place this application in condition for allowance. If any fees are due for consideration of this Response, the Office is expressly authorized to charge those fees to Deposit Account No. 03-0172.

Respectfully submitted,

Date: March 9, 2004

By: 

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